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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/444,095	11/22/99	IBRAHIM S	ARMY-123

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EXAMINER	
SISSON, B	
ART UNIT	**PAPER NUMBER**
1655	11

DATE MAILED: 11/07/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/444,095	SOFI, IBRAHIM M.	
	Examiner	Art Unit	
	Bradley L. Sisson	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *25 September 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-35,38,39 and 63-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-35,38,39 and 63-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 31-35, and 63-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of binding nucleic acids and proteins to a support in a non-specific manner (not predicated on the sequence of nucleotides or amino acids), does not reasonably provide enablement for sequence-specific binding of nucleic acids or proteins nor for conducting an amplification reaction followed by specific or non-specific binding of nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. As presently worded the method of claims 31-35, 38, 39, and 63-67 has sufficient breadth of scope so to encompass specific isolation/binding of target nucleic acids or proteins to a solid support. Indeed, claims 63-67 are directed to just such a method. As set forth in the preamble of claim 31, the denaturing solution does not give rise to denatured nucleic acids, be they DNA or RNA. Yet, in order for one to selectively bind a probe to target nucleic acids, there needs to be a denaturation of the target nucleic acid such that it is single stranded prior to hybridizing to the probe to the target. The specification has been found to contain suggestions that the hybridization step can be conducted subsequent to having performed polymerase chain reaction. Neither the claims nor the specification teach how one is

to perform such an amplification reaction when the nucleic acid is present in a protein denaturing solution. Clearly, without something being done to the denaturation solution in which one finds the crude nucleic acid sample, the polymerase used to perform an amplification reaction would be rendered denatured and as a direct result of such, be rendered inoperative.

3. Newly added claims 63-67 apparently seek to overcome some of the identified shortcomings identified in the prior Office action. However, the specification is essentially silent as to how the method is to be practiced. It is noted with particularity that the specification does not provide any examples as to how such denaturation and annealing are to occur or to how prior art methods are to be adapted to the current method. Further, the claimed invention relates directly to matters of physiology and chemistry, which are inherently unpredictable and as such, require greater levels of enablement. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

> In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

4. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
>
> *****

> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

5. It appears that the burden of enabling the full scope of the invention is to be shifted to the public and not be born by applicant. The specification, as shown above, provides for but limited guidance. To force the public to determine the operational parameters and requirements for a system that deals with a area of technology recognized by the Court as being unpredictable would constitute an unfair shifting of the burden to disclose.

Response to Arguments

6. At page 3 of the response received 25 September 2000 applicant directs attention to a number of publications and asserts that such documents are representative of the state of the art.

The documents provided in the listing have not been considered on the record as they have not been provided on a PTO-1449 (Information Disclosure Statement) accompanied with

the requisite certification and/or fee. Further, such documents, even if submitted, would not be considered as evidence of the state of the art as such do not take the form of a sworn declaration. Further, even if a sworn statement were to be provided that the cited documents are representative of the state of the art, the specification is still considered to be essentially silent as to how a skilled artisan would adapt the prior art method to the manipulation and employment of the device required in the claimed methods.

7. At page 4 of the response received 25 September 2000, it is asserted that the claims have been interpreted out of context and that the specification is enabling for claims 31-35.

The above argument has been fully considered and has not been found to be persuasive towards the withdrawal of the rejection. As noted by applicant in their response, the specification does make reference to modification and application of the method to additional embodiments including "incorporating thermal cycling amplification (e.g., PCR), isothermal amplification and fluoregenic [*sic*], colorimetric, luminescence or electrochemical detection in the same device." While the claims are read in light of the specification, proffered limitations as to what the claims are not to encompass are not read into the claims. It is noted with particularity that the method of claim 31 and by default, claims 32-35, 38, and 39 which depend therefrom, employ a "sample collection assembly" just as newly added claim 63 employs wherein the method of claim 63 (and dependent claims 64-67) is directed to "[a] method of capturing specific DNA or RNA."

Claims 31-35, like newly added claims 63-67, are not adequately supported by the disclosure to the extent that one of skill in the art would be able to practice the full scope of the claimed method less resort to undue experimentation to do so.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 65-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. The term "several" in claim 65 is a relative term that renders the claim indefinite. The term "several" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

11. The term "deep" in claims 6 and 67 is a relative term that renders the claims indefinite. The term "deep" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

12. The term "vast" in claims 66 and 67 is a relative term that renders the claims indefinite. The term "vast" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

13. Claims 31-35 and 63-67 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are:

a. How the nucleic acid is to be prepared such that it is used in a hybridization reaction;

b. If one is to conduct an amplification reaction, just how the amplification reaction is to be performed while there is a protein denaturant present (seemingly, the protein denaturant will result in rendering the polymerase inoperative). If one is to use a peptide p[robe after amplification, and the peptide probe is an anti-histone antibody, the method needs to reflect what steps are needed so to render the amplified nucleic acid capable of being bound by the antibody, if such is even possible; and

c. Like "b", *supra*, the use of a peptide probe, e.g., an antibody, to bind the nucleic acid, while the protein denaturant is present, raises several issues. The claims need to reflect just what steps are need so to render the sample mixture susceptible to binding by another protein when the presence of the denaturant would result in the denaturation of the peptide probe.

Response to Arguments

At page 5 of the response it is asserted that "a hybridization reaction is not the subject matter of claims 31-35" and as such, no additional method steps are necessary.

The above argument has bee fully considered and has not been found to be persuasive towards the withdrawal of the rejection. Attention is directed to claim 31, fourth paragraph, which teaches specifically of denaturing the sample DNA or RNA and allowing same to bind to the "sample collection assembly." At page 7 of the specification it is disclosed that the "sample capture assembly" is ultimately "coated with a target specific surface such as specific oligonucleotides, peptides or cell receptors to capture a target DNA, RNA, or protein or cell

type." Given that the claimed method is limited to the "DNA or RNA purification" the "sample capture assembly" has not been interpreted as being directed to the capture of protein or cell type which in turn leaves the capture of DNA or RNA. Clearly, if the "sample collection assembly" is to capture DNA or RNA via the use of oligonucleotides, such must be accomplished via hybridization. Accordingly, the previously identified method steps are still deemed essential.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 31-35, 38, 39 and 63-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ji et al., in view of Henco et al., Piaso et al., Lockhart et al., Tuunanen (WO 94/18564).

Ji et al., disclose a method for the isolation of nucleic acid from a lysate solution. As set forth in columns 3 and 4, the solid support can be of virtually any shape and that the capture sequence could be immobilized on a support that can be of "column packing material" as well as filter paper support. The use of magnetic beads as a suitable support is disclosed in column 4, fifth paragraph, and in the sixth paragraph, the use of wash solutions so to remove unwanted lysate materials is similarly disclosed.

Ji et al., do not teach explicitly of the use of a wand that has a surface that would bind to the nucleic acid in the lysate solution.

Henco et al., disclose the use of silica gel particles that are trapped in a network of membranes for the binding/isolation of nucleic acids from a cellular lysate solution. Column 3, penultimate paragraph, discloses the washing of contaminates out of the microparticles and the subsequent elution of the bound nucleic acid from the solid support [applicant's sample collection assembly]. The aspect of performing polymerase chain reaction is disclosed at column 3, penultimate paragraph.

Piasio et al., disclose a variety of solid support shapes that can be used in any number of binding reactions; see Figures 1-6. As seen in the Figures, the support surfaces are attached to a wand that can be inserted into a tube into which is placed a sample solution. A common feature of the support surface is the presence of a binding member and the large amount of surface area each of the support surfaces provides, thereby increasing the efficiency of the solid support to bind the target ligand. Column 3, penultimate paragraph, discloses the use of glass beads as a solid support to which the analyte of interest is bound. The use of glass speaks directly to the presence of silicon oxide.

Lockhart et al., disclose the binding of nucleic acid to a solid support. Columns 7 through 9 speak to innumerable types and shapes of solid supports as well as the associated functional groups, including silicon oxide.

Tuunanen disclose a device used in binding reactions where a solid support is attached to a wand. The wand and associated solid support is inserted into a tube that has a sample solution so to effect binding. The wand/solid support, with its associated handle, is then passed on to a series of other tubes containing additional solutions. As seen in Figures 1 and 2, elements 4 and 4.1 respectively depict various solid supports. As set forth in page 6, third paragraph, an

advantage in having an increased surface area is addressed. Similarly, at page 5, first paragraph, the "body surface [applicant's sample collection assembly] has suitable protrusions and cavities 7 to increase the surface area. In this embodiment [Figure 1] they are grooves leading toward the point." Page 5, second paragraph, speaks directly to the use of multiple washing steps which are in additional tubes.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have combined the teachings of Ji et al., with that of Piasio et al., Henco et al., Lockhart et al., and Tuunanen so as to arrive at a method of binding nucleic acid in a lysate solution wherein said binding is effected by a device comprising a sample collection assembly attached to a wand or shaft that is in turn attached to a cap wherein the cap/wand/sample collection assembly is inserted into a tube so as to permit the binding of nucleic acids to the sample collection assembly and is subsequently subject to a series of washing steps prior to the elution or removal of the nucleic acid from the sample collection assembly. The ordinary artisan would have been motivated to have devised a sample collection assembly that maximized surface area for as shown in the prior art of record, such was already a motivating force as an increase in surface area permitted higher ratios of contact between the sample and the solid support and the related binding of the nucleic acid to the solid support as a direct result of the nucleic acid having been brought into contact with the support. For the above reasons, and in the absence of convincing evidence to the contrary, the claimed invention has been found to have been reasonably suggested by the prior art of record and in view of the well developed nature of the subject matter to which the invention relates, the ordinary artisan would have had a reasonable expectation for success.

Response to Arguments

15. Applicant's arguments filed 25 September 2000 have been fully considered but they are not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a method that employs an apparatus for the purification and concentration of nucleic acids such as DNA or RNA from a sample without the need for centrifugation, precipitation, lengthy incubations, magnetic fields or gravity (page 6 of the response); not requiring cell immobilization for fixing DNA through a column or column matrix (page 7 of the response); or the use of a smooth surface (response at page 7)) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

For the above reasons, and in the absence of convincing evidence to the contrary, the rejection is maintained against claims 31-35, 38, 39 and is also applied against newly added claims 63-67.

Conclusion

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1655

BLS
November 4, 2000